cl 7(6).

```
     (FILE 'HOME' ENTERED AT 13:16:28 ON 02 DEC 2004)

     FILE 'CAPLUS, MEDLINE' ENTERED AT 13:18:11 ON 02 DEC 2004
L1            81 FILE CAPLUS
L2           140 FILE MEDLINE
     TOTAL FOR ALL FILES
L3           221 S ((HIV (3W) (REVERSE TRANSCRIPTASE)) OR NTRI) AND RESISTANCE A
L4             1 FILE CAPLUS
L5             1 FILE MEDLINE
     TOTAL FOR ALL FILES
L6             2 S L3 AND (184 (3A) ((G OR GLY)  OR (L OR LEU)))

     FILE 'CAPLUS' ENTERED AT 13:56:29 ON 02 DEC 2004
L7             4 S (129:15939 OR 124:219374 OR 123:74260 OR 122:230221)/DN

     FILE 'CAPLUS, MEDLINE' ENTERED AT 14:09:40 ON 02 DEC 2004
L8             1 FILE CAPLUS
L9             0 FILE MEDLINE
     TOTAL FOR ALL FILES
L10            1 S L3 AND (215 (3A) ((V OR VAL) ))
L11            0 FILE CAPLUS
L12            0 FILE MEDLINE
     TOTAL FOR ALL FILES
L13            0 S L3 AND (118 (3A) ((I OR ILE) ))
L14            3 FILE CAPLUS
L15            2 FILE MEDLINE
     TOTAL FOR ALL FILES
L16            5 S L3 AND (44 (3A) ((A OR ALA) OR (D OR GLU)))
L17            1 DUPLICATE REMOVE L6 (1 DUPLICATE REMOVED)
```

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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 01   INPADOC: New family current-awareness alert (SDI) available
 NEWS  4  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS  5  SEP 01   New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
 NEWS  6  SEP 27   STANDARDS will no longer be available on STN
 NEWS  7  SEP 27   SWETSCAN will no longer be available on STN
 NEWS  8  OCT 28   KOREAPAT now available on STN
 NEWS  9  NOV 18   Current-awareness alerts, saved answer sets, and current
                   search transcripts to be affected by CERAB, COMPUAB, ELCOM,
                   and SOLIDSTATE reloads
 NEWS 10  NOV 30   PHAR reloaded with additional data
 NEWS 11  DEC 01   LISA now available on STN

 NEWS EXPRESS  OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:16:28 ON 02 DEC 2004

=> file caplus,medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.63       0.63

FILE 'CAPLUS' ENTERED AT 13:18:11 ON 02 DEC 2004
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FILE 'MEDLINE' ENTERED AT 13:18:11 ON 02 DEC 2004

=> s ((HIV (3w) (reverse transcriptase)) or NTRI) and resistance and (44 or 69 or 118 or 184)
L1           81 FILE CAPLUS
L2          140 FILE MEDLINE

TOTAL FOR ALL FILES
L3          221 ((HIV (3W) (REVERSE TRANSCRIPTASE)) OR NTRI) AND RESISTANCE AND
                (44 OR 69 OR 118 OR 184)
```

```
=> duplicate remove
ENTER L# LIST OR (END):l3
DUPLICATE PREFERENCE IS 'CAPLUS, MEDLINE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L3
L4          152 DUPLICATE REMOVE L3 (69 DUPLICATES REMOVED)

=> del l4
DELETE L4? (Y)/N:y

=> s l3 and (184 (3a) ((G or Gly)  or (L or Leu))
UNMATCHED LEFT PARENTHESIS 'AND (184'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l3 and (184 (3a) ((G or Gly)  or (L or Leu)))
L4            1 FILE CAPLUS
L5            1 FILE MEDLINE

TOTAL FOR ALL FILES
L6            2 L3 AND (184 (3A) ((G OR GLY) OR (L OR LEU)))

=> d

L6   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
Full Text
AN   1996:491295  CAPLUS
DN   125:189243
TI   Mutational studies of human immunodeficiency virus type 1 reverse
     transcriptase: the involvement of residues 183 and 184 in the fidelity
     of DNA synthesis
AU   Bakhanashvili, Mary; Avidan, Orna; Hizi, Amnon
CS   Department of Cell Biology and Histology, Sackler School of Medicine, Tel
     Aviv University, Tel Aviv-Jaffa, 69978, Israel
SO   FEBS Letters (1996), 391(3), 257-262
     CODEN: FEBLAL; ISSN: 0014-5793
PB   Elsevier
DT   Journal
LA   English


=> d bib,abs

L6   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
Full Text
AN   1996:491295  CAPLUS
DN   125:189243
TI   Mutational studies of human immunodeficiency virus type 1 reverse
     transcriptase: the involvement of residues 183 and 184 in the fidelity
     of DNA synthesis
AU   Bakhanashvili, Mary; Avidan, Orna; Hizi, Amnon
CS   Department of Cell Biology and Histology, Sackler School of Medicine, Tel
     Aviv University, Tel Aviv-Jaffa, 69978, Israel
SO   FEBS Letters (1996), 391(3), 257-262
     CODEN: FEBLAL; ISSN: 0014-5793
PB   Elsevier
DT   Journal
LA   English
AB   The high error rates characteristic of human immunodeficiency virus type-1
     reverse transcriptase (HIV-1 RT) are a presumptive source of the viral
     hypermutability that impedes prevention and therapy of acquired
     immunodeficiency syndrome (AIDS).  We have analyzed two mutants of HIV-1
```

RT by conducting a comparative study of the accuracy of DNA synthesis. Each mutant bears a single amino acid substitution adjacent to the two aspartic acid residues at positions 185 and 186 in the highly conserved DNA polymerase active site. The first mutant, Met **184→Leu** (M184L), displays a marked redn. in both misinsertion and mispair extension, suggesting a fidelity of DNA synthesis significantly higher than that of the wild-type HIV-1 RT. The second mutant, Tyr 183→Phe (Y183F), shows a decrease in mispair extension with no significant change in misincorporation. Thus, the overall pattern of error-proneness of DNA synthesis is: wild-type HIV-1 RT > Y183F > M184L. Taken together, it is possible that residues 183 and **184** contribute to the low fidelity of DNA synthesis characteristic of the reverse transcriptases of HIV-1, HIV-2 and possibly, of other lentiviruses. Our observations may bear on the nature of potential mutations responsible for **resistance** to the nucleoside analogs used in chemotherapy of AIDS.

=> d au,so

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AU Bakhanashvili, Mary; Avidan, Orna; Hizi, Amnon
SO FEBS Letters (1996), 391(3), 257-262
CODEN: FEBLAL; ISSN: 0014-5793

=> d au,so

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AU Bakhanashvili, Mary; Avidan, Orna; Hizi, Amnon
SO FEBS Letters (1996), 391(3), 257-262
CODEN: FEBLAL; ISSN: 0014-5793

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	57.75	58.38

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.70	-0.70

FILE 'CAPLUS' ENTERED AT 13:56:29 ON 02 DEC 2004
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FILE COVERS 1907 - 2 Dec 2004 VOL 141 ISS 23
FILE LAST UPDATED: 1 Dec 2004 (20041201/ED)

This file contains CAS Registry Numbers for easy and accurate

substance identification.

```
=> s (129:15939 or 124:219374 or 123:74260 or 122:230221)/dn
             1 129:15939/DN
             1 124:219374/DN
             1 123:74260/DN
             1 122:230221/DN
L7           4 (129:15939 OR 124:219374 OR 123:74260 OR 122:230221)/DN

=> d au,so 1-4

L7   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
AU   Cushman, Mark; Casimiro-Garcia, Agustin; Hejchman, Elzbieta; Ruell,
     Jeffrey A.; Huang, Mingjun; Schaeffer, Catherine A.; Williamson, Karen;
     Rice, William G.; Buckheit, Robert W., Jr.
SO   Journal of Medicinal Chemistry (1998), 41(12), 2076-2089
     CODEN: JMCMAR; ISSN: 0022-2623

L7   ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
AU   Buckheit, Robert W., Jr.; Kinjerski, Tracy L.; Fliakas-Boltz, Valerie;
     Russell, Julie D.; Stup, Tracy L.; Pallansch, Luke A.; Brouwer, Walter G.;
     Dao, Dong C.; Harrison, W. Ashley; et al.
SO   Antimicrobial Agents and Chemotherapy (1995), 39(12), 2718-27
     CODEN: AMACCQ; ISSN: 0066-4804

L7   ANSWER 3 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
AU   Buckheit, Robert W., Jr.; Fliakas-Boltz, VAlerie; Yeagy-Bargo, Sharon;
     Weislow, Owen; Mayers, Douglas L.; Boyer, Paul L.; Hughes, Stephen H.;
     Pan, Bai-Chuan; Chu, Shih-Hsi; et al.
SO   Virology (1995), 210(1), 186-93
     CODEN: VIRLAX; ISSN: 0042-6822

L7   ANSWER 4 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
AU   Seki, M.; Sadakata, Y.; Yuasa, S.; Baba, M.
SO   Antiviral Chemistry Chemotherapy (1995), 6(2), 73-9
     CODEN: ACCHEH; ISSN: 0956-3202


=> d dn,au,so 1-4

L7   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
DN   129:15939
AU   Cushman, Mark; Casimiro-Garcia, Agustin; Hejchman, Elzbieta; Ruell,
     Jeffrey A.; Huang, Mingjun; Schaeffer, Catherine A.; Williamson, Karen;
     Rice, William G.; Buckheit, Robert W., Jr.
SO   Journal of Medicinal Chemistry (1998), 41(12), 2076-2089
     CODEN: JMCMAR; ISSN: 0022-2623

L7   ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
DN   124:219374
AU   Buckheit, Robert W., Jr.; Kinjerski, Tracy L.; Fliakas-Boltz, Valerie;
     Russell, Julie D.; Stup, Tracy L.; Pallansch, Luke A.; Brouwer, Walter G.;
     Dao, Dong C.; Harrison, W. Ashley; et al.
SO   Antimicrobial Agents and Chemotherapy (1995), 39(12), 2718-27
     CODEN: AMACCQ; ISSN: 0066-4804

L7   ANSWER 3 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
DN   123:74260
AU   Buckheit, Robert W., Jr.; Fliakas-Boltz, VAlerie; Yeagy-Bargo, Sharon;
     Weislow, Owen; Mayers, Douglas L.; Boyer, Paul L.; Hughes, Stephen H.;
     Pan, Bai-Chuan; Chu, Shih-Hsi; et al.
```

SO Virology (1995), 210(1), 186-93
CODEN: VIRLAX; ISSN: 0042-6822

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
DN **122:230221**
AU Seki, M.; Sadakata, Y.; Yuasa, S.; Baba, M.
SO Antiviral Chemistry Chemotherapy (1995), 6(2), 73-9
CODEN: ACCHEH; ISSN: 0956-3202

=> d4 bib,abs
D4 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d 4 bib,abs

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 1995:445027 CAPLUS
DN **122:230221**
TI Isolation and characterization of human immunodeficiency virus type-1 mutants resistant to the non-nucleotide reverse transcriptase inhibitor MKC-442
AU Seki, M.; Sadakata, Y.; Yuasa, S.; Baba, M.
CS Laboratory of Bioscience, Mitsubishi Kasei Corp., Yokohama, 227, Japan
SO Antiviral Chemistry Chemotherapy (1995), 6(2), 73-9
CODEN: ACCHEH; ISSN: 0956-3202
PB Blackwell
DT Journal
LA English
AB MKC-442, 6-benzyl-1-ethoxymethyl-5-isopropyluracil (I-EBU), is a potent and selective non-nucleoside inhibitor of human immunodeficiency virus type-1 (HIV-1) reverse transcriptase (RT). Nevirapine, another non-nucleoside RT inhibitor (NNRTI), is assocd. with rapid emergence of drug-resistant variants during in vitro passages of HIV-1. The emergence of resistant viruses to MKC-442 or nevirapine was examd. in vitro. MT-4 cells infected with a clin. isolate (HE) of HIV-1 were cultivated in medium contg. excess concns. of these drugs, and the drug susceptibilities of the breakthrough viruses recovered from the medium were measured. Although nevirapine lost its antiviral activity after six passages, a delay in the emergence of fully resistant viruses was obsd. for MKC-442. Two resistant clones for each drug were isolated and nucleotide sequences within the RT region were analyzed. An amino acid substitution at position 181 (Tyr to Cys) was found, with addnl. substitutions at positions 103 (Lys to Arg) and 108 (Val to Ile) in the MKC-442-resistant viruses. These clones showed various susceptibilities to MKC-442, and cross-resistance to other NNRTIs but not to AZT. These results suggest that the major binding site of MKC-442 on the HIV-1 RT is the tyrosine residue common to these NNRTIs, and that drug resistance to NNRTIs is dependent on both the quality and the quantity of mutations within the HIV-1 RT gene.

=> d his

(FILE 'HOME' ENTERED AT 13:16:28 ON 02 DEC 2004)

FILE 'CAPLUS, MEDLINE' ENTERED AT 13:18:11 ON 02 DEC 2004
L1 81 FILE CAPLUS
L2 140 FILE MEDLINE

```
     TOTAL FOR ALL FILES
L3           221 S ((HIV (3W) (REVERSE TRANSCRIPTASE)) OR NTRI) AND RESISTANCE A
L4             1 FILE CAPLUS
L5             1 FILE MEDLINE
     TOTAL FOR ALL FILES
L6             2 S L3 AND (184 (3A) ((G OR GLY)  OR (L OR LEU)))

     FILE 'CAPLUS' ENTERED AT 13:56:29 ON 02 DEC 2004
L7             4 S (129:15939 OR 124:219374 OR 123:74260 OR 122:230221)/DN

=> file caplus,medline
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        27.99      86.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                        -0.70      -1.40

FILE 'CAPLUS' ENTERED AT 14:09:40 ON 02 DEC 2004
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FILE 'MEDLINE' ENTERED AT 14:09:40 ON 02 DEC 2004

=> s l3 and (215 (3a) ((V or Val) ))
L8             1 FILE CAPLUS
L9             0 FILE MEDLINE

TOTAL FOR ALL FILES
L10            1 L3 AND (215 (3A) ((V OR VAL) ))

=> d

L10  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
Full Text
AN   2000:712654  CAPLUS
DN   133:262274
TI   HIV protease and reverse transcriptase gene mutation detection
     method via PCR and hybridization
IN   Shimada, Kazunori
PA   Genome Science Kenkyusho K. K., Japan
SO   Jpn. Kokai Tokkyo Koho, 19 pp.
     CODEN: JKXXAF
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ----------------    ----   --------    --------------------    --------
PI   JP 2000279197        A2    20001010    JP 1999-92269           19990331
PRAI JP 1999-92269                19990331


=> s l3 and (118 (3a) ((I or Ile) ))
L11            0 FILE CAPLUS
L12            0 FILE MEDLINE

TOTAL FOR ALL FILES
L13            0 L3 AND (118 (3A) ((I OR ILE) ))

=> s l3 and (44 (3a) ((A or Ala) or (D or Glu))
```

```
UNMATCHED LEFT PARENTHESIS 'AND (44'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l3 and (44 (3a) ((A or Ala) or (D or Glu)))
L14             3 FILE CAPLUS
L15             2 FILE MEDLINE

TOTAL FOR ALL FILES
L16             5 L3 AND (44 (3A) ((A OR ALA) OR (D OR GLU)))

=> duplicate remove n
ENTER L# LIST OR (END):l16
'N' IS NOT VALID.  VALID FILE NAMES ARE 'CAPLUS, MEDLINE'
You have entered a file name of duplicates to keep that is not
referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.
ENTER FILE NAMES OF DUPLICATES TO KEEP:end

=> duplicate remove l6
DUPLICATE PREFERENCE IS 'CAPLUS, MEDLINE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L6
L17             1 DUPLICATE REMOVE L6 (1 DUPLICATE REMOVED)

=> d l16 bib,kwic 1-5

L16  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
Full Text
AN   2003:986848  CAPLUS
DN   141:116470
TI   An open-label assessment of TMC 125-a new, next-generation NNRTI, for 7
     days in HIV-1 infected individuals with NNRTI resistance
AU   Gazzard, Brian G.; Pozniak, Anton L.; Rosenbaum, Willy; Yeni, G. Patrick;
     Staszewski, Schlomo; Arasteh, Keikawus; De Dier, Karin; Peeters, Monika;
     Woodfall, Brian; Stebbing, Justin; van't Klooster, Gerben A.
CS   Chelsea and Westminster Hospital, London, UK
SO   AIDS (London, United Kingdom) (2003), 17(18), F49-F54
     CODEN: AIDSET; ISSN: 0269-9370
PB   Lippincott Williams Wilkins
DT   Journal
LA   English
RE.CNT  15    THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI   An open-label assessment of TMC 125-a new, next-generation NNRTI, for 7
     days in HIV-1 infected individuals with NNRTI resistance
AB   Summary: The development of resistance to any of the currently licensed
     non-nucleoside reverse transcriptase inhibitors (NNRTI) invariably leads
     to cross-resistance to the drugs in that class.  New NNRTI, that have
     the promise of being active even when such 'signature' mutations are
     present, are in development.  Such novel therapies could be effective
     after current NNRTI failure as there would probably be no
     cross-resistance.  We assessed the short-term efficacy and safety of a
     next generation NNRTI, TMC 125, a diarylpyrimidine deriv. that has in
     vitro activity against NNRTI resistant HIV-1.  TMC 125 was studied in
     HIV-1 infected patients with high-level phenotypic NNRTI resistance in
     an open-label phase IIa trial.  Methods: Sixteen individuals receiving an
     NNRTI-contg. antiretroviral regimen (efavirenz or nevirapine) with an
     HIV-1 RNA viral load of > 2000 copies/mL and phenotypic resistance to
     NNRTI, received TMC 125 for 7 days, as a substitute for their current
     NNRTI in their failing therapy.  Full pharmacokinetic profiles were
```

investigated. Findings: The primary end point-viral load decay rate per day - was 0.13 log10 RNA copies/mL per day. Over 7 days, we obsd. a median 0.89 log10 decrease in HIV-1 viral load; seven individuals (**44%**) had **a** decrease of > 1 log1010. The most significant adverse effects were grade I diarrhea (31%) and a mild headache (25%). Steady-state drug levels were achieved by day 6. Interpretation: TMC 125, a next generation NNRTI, is well tolerated and demonstrates significant and rapid antiviral activity in patients with high levels of phenotypic NNRTI **resistance** to current NNRTI.

ST non nucleoside reverse transcriptase inhibitor TMC125 pharmacokinetics HIV antiAIDS; antiviral **resistance HIV** antiAIDS non nucleoside **reverse transcriptase** inhibitor

IT Drug **resistance**
(antiviral; new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

IT Anti-AIDS agents
Human
Human immunodeficiency virus 1
Phenotypes
(new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

IT Viral RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

IT Antiviral agents
(**resistance** to; new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

IT 269055-15-4, TMC 125
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

IT 129618-40-2, Nevirapine 136817-59-9, Delavirdine 154598-52-4, Efavirenz
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new generation NNRTI TMC-125 is well tolerated with significant antiviral activity in HIV-1 patient even in presence of mutations conferring high level of phenotypic **resistance** to efavirenz and nevirapine)

L16 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 2000:511498 CAPLUS
DN 134:80517
TI Evolution of lamivudine-resistant hepatitis B virus and HIV-1 in co-infected individuals. An analysis of the CAESAR study
AU Pillay, Deenan; Cane, Patricia A.; Ratcliffe, Daina; Atkins, Mark; Cooper, David
CS CAESAR Co-ordinating Committee, Public Health Laboratory Service Antiviral Susceptibility Reference Unit, Division of Immunity and Infection,

University of Birmingham Medical School, Edgbaston, B15 2TT, UK
SO AIDS (London) (2000), 14(9), 1111-1116
CODEN: AIDSET; ISSN: 0269-9370
PB Lippincott Williams Wilkins
DT Journal
LA English
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Lamivudine has potent activity against HIV-1 and hepatitis B virus (HBV). Co-infection with these 2 viruses is common, and this may therefore influence the choice of antiretroviral therapies. A cohort of co-infected patients treated with lamivudine were studied to evaluate the differential effects of lamivudine on the 2 viral populations within the same individual after **44**-52 wk of therapy. Retrospective virol. anal. of an HIV-1/HBV co-infected lamivudine cohort derived from a randomized, placebo-controlled study of lamivudine in HIV infection, the CAESAR study. 5 Of 13 patients with HBV viral load >10,000 copies/mL after **44**-52 wk of lamivudine therapy had genotypic drug **resistance**. 4 Of these 5 had a rebound of viral replication over the period of study and in 1 case this was assocd. with an alanine transaminase serum elevation. 10 Of the 13 patients had **a 44**-52 wk HIV viral load >1000 copies/mL, all of whom also had **HIV reverse transcriptase** M184V or M184I mutations. Extrapolating these results to the population yields an estd. 1-yr incidence of drug-resistant HBV of at least 14% in lamivudine-treated HIV-1/HBV co-infected patients. The clin. and virol. benefit of HBV lamivudine monotherapy in co-infected patients should be balanced against the potential for emergence of drug **resistance**. Further, these data suggest that the determinants of HIV and HBV drug **resistance** are different and that parallel evolution, rather than co-evolution of HBV and HIV-1 in co-infected individuals occurs.
ST lamivudine drug **resistance** hepatitis B virus HIV
IT Antiviral agents
(**resistance** to; lamivudine-resistant hepatitis B virus and HIV-1 in co-infected individuals)

L16 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 1996:568526 CAPLUS
DN 125:264641
TI Nevirapine: a review of its development, pharmacological profile and potential for clinical use
AU Murphy, Robert L.; Montaner, Julio
CS Northwestern University, Chicago, IL, USA
SO Expert Opinion on Investigational Drugs (1996), 5(9), 1183-1199
CODEN: EOIDER; ISSN: 0967-8298
PB Ashley Publications
DT Journal; General Review
LA English
AB **A** review with **44** refs. Nevirapine, a dipyridodiazepinone, is the prototypic member of a class of antiretroviral compds. referred to as nonnucleoside reverse transcriptase inhibitors. Nevirapine is a potent and selective noncompetitive inhibitor of the reverse transcriptase enzyme, an important therapeutic target for the treatment of HIV-1 infection. The activity of nevirapine does not compete with template or nucleoside triphosphates, nor does it inhibit **HIV**-2 **reverse transcriptase** or any of the human DNA polymerases. In completed clin. studies, nevirapine has demonstrated antiretroviral activity both as monotherapy and in combination with nucleoside analogs. When administered with zidovudine or the combination zidovudine/didanosine, the antiviral effect has been profound and sustained. A favorable antiviral effect and CD4!+ lymphocyte response has been demonstrated in both adults and children, in patients experienced and naive to antiretroviral therapy as

well as in those with baseline **resistance** to zidovudine. Nevirapije has a favorable pharmacokinetic profile, becomes widely distributed throughout body tissues including the central nervous system, and is active in the adult at an oral dose of 200 mg administered twice daily after a two week leak-in dose of 200 mg per day. There are no significant drug-drug interactions noted with the nucleoside reverse transcriptase inhibitors; however, because nevirapine induces cytochrome P 450 isoenzymes, the currently used protease inhibitors may undergo more rapid rates of metab. Other commonly used drugs, such as ketoconazole, depsone, rifampin, rifabutin and trimethoprim-sulfamethoxazole, appear not to be significantly affected. **Resistance** to nevirapine is rapid when administered as a monotherapy but this is altered and made less clin. relevant when nevirapine is given in combination with one or more of the nucleosides. Nevirapine has a safety profile that does not overlap with overlap with other antiretroviral therapies, the most common treatment-limiting reaction being rash. Nevirapine is an active antiretroviral agent with excellent biodistribution and good potential for use in combination with other antiretrovirals across the spectrum of HIV disease as well as in selected populations.

L16 ANSWER 4 OF 5 MEDLINE on STN
Full Text
AN 2001571617 MEDLINE
DN PubMed ID: 11679154
TI HIV type 1 genetic diversity is a major obstacle for antiretroviral drug **resistance** hybridization-based assays.
AU Kijak G H; Rubio A E; Quarleri J F; Salomon H
CS National Reference Center for AIDS, Department of Microbiology, School of Medicine, University of Buenos Aires, 1121 Buenos Aires, Argentina.
SO AIDS research and human retroviruses, (2001 Oct 10) 17 (15) 1415-21. Journal code: 8709376. ISSN: 0889-2229.
CY United States
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LA English
FS Priority Journals; AIDS
OS GENBANK-AF360751; GENBANK-AF360752; GENBANK-AF360753; GENBANK-AF360754; GENBANK-AF360755; GENBANK-AF360756; GENBANK-AF360757; GENBANK-AF360758; GENBANK-AF360759; GENBANK-AF360760; GENBANK-AF360761; GENBANK-AF360762; GENBANK-AF360763; GENBANK-AF360764; GENBANK-AF360765; GENBANK-AF360766; GENBANK-AF360767; GENBANK-AF360768; GENBANK-AF360769; GENBANK-AF360770; GENBANK-AF360771; GENBANK-AF360772; GENBANK-AF360773; GENBANK-AF360774; GENBANK-AF360775; GENBANK-AF360776; GENBANK-AF360777; GENBANK-AF360778; GENBANK-AF360779; GENBANK-AF360780; GENBANK-AF360781; GENBANK-AF360782; GENBANK-AF360783; GENBANK-AF360784; GENBANK-AF360785; GENBANK-AF360786; GENBANK-AF360787; GENBANK-AF360788; GENBANK-AF360789; GENBANK-AF360790; GENBANK-AF360791; GENBANK-AF360792; GENBANK-AF360793; GENBANK-AF360794; GENBANK-AF360795; GENBANK-AF360796; GENBANK-AF360797; GENBANK-AF360798; GENBANK-AF360799; GENBANK-AF360800; GENBANK-AF360801; GENBANK-AF360802; GENBANK-AF360803; GENBANK-AF360804; GENBANK-AF360805; GENBANK-AF360806; GENBANK-AF360807; GENBANK-AF360808; GENBANK-AF360809; GENBANK-AF360810; GENBANK-AF360811; GENBANK-AF360812; GENBANK-AF360813; GENBANK-AF360814; GENBANK-AF360815; GENBANK-AF360816; GENBANK-AF360817; GENBANK-AF360818; GENBANK-AF360819; GENBANK-AF360820; GENBANK-AF360821; GENBANK-AF360822; GENBANK-AF360823; GENBANK-AF360824; GENBANK-AF360825; GENBANK-AF360826; GENBANK-AF360827; GENBANK-AF360828; GENBANK-AF360829; GENBANK-AF360830; GENBANK-AF360831; GENBANK-AF360832; GENBANK-AF360833; GENBANK-AF360834; GENBANK-AF360835; GENBANK-AF360836; GENBANK-AF360837; GENBANK-AF360838; GENBANK-AF360839; GENBANK-AF360840; GENBANK-AF360841; GENBANK-AF360842; GENBANK-AF360843
EM 200112
ED Entered STN: 20011029
Last Updated on STN: 20020222

Entered Medline: 20011221

TI HIV type 1 genetic diversity is a major obstacle for antiretroviral drug **resistance** hybridization-based assays.

AB Human immunodeficiency virus type 1 (HIV-1) is characterized by high genetic diversity. Current antiretroviral (ARV) drug **resistance** genotyping assays have been designed on the basis of the most prevalent sequence patterns circulating in the United States and. . . genetic diversity of HIV-1 forms circulating in Argentina and the lack of reactivity at codon 74 in an ARV drug **resistance** hybridization-based assay. Samples taken from 93 HIV-1-infected individuals of Buenos Aires, Argentina were studied. The reverse transcriptase (RT) region of. . . recombination analyses were carried out, showing that 52 of 93 (55.9%) samples belonged to subtype B, whereas 41 of 93 (**44**.1%) showed **a** (5') F1/B (3') subtype recombinant genomic structure. For codon 74 in the LiPA test, 4 of 52 (7.7%) B-subtype samples. . . recombinant samples ($p < 0.001$). The present data indicate that HIV-1 genetic diversity is a major obstacle for ARV drug **resistance** hybridization-based assays.

CT Check Tags: Human; Support, Non-U.S. Gov't
Base Sequence
DNA, Viral
***Drug Resistance, Viral: GE, genetics**
HIV-1: CL, classification
*HIV-1: GE, genetics
***HIV-1 Reverse Transcriptase: GE, genetics**
Molecular Sequence Data
Nucleic Acid Hybridization: MT, methods
Phylogeny
Recombination, Genetic
*Variation (Genetics)

CN 0 (DNA, Viral); EC 2.7.7.- (**HIV-1 Reverse Transcriptase**)

L16 ANSWER 5 OF 5 MEDLINE on STN
Full Text

AN 2001009355 MEDLINE

DN PubMed ID: 10894274

TI Evolution of lamivudine-resistant hepatitis B virus and HIV-1 in co-infected individuals: an analysis of the CAESAR study. CAESAR co-ordinating committee.

AU Pillay D; Cane P A; Ratcliffe D; Atkins M; Cooper D

CS Division of Immunity and Infection, University of Birmingham Medical School, Edgbaston, UK.. D.Pillay@bham.ac.uk

SO AIDS (London, England), (2000 Jun 16) 14 (9) 1111-6.
Journal code: 8710219. ISSN: 0269-9370.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)

LA English

FS Priority Journals; AIDS

EM 200010

ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001025

AB . . . studied in order to evaluate the differential effects of lamivudine on the two viral populations within the same individual after **44**-52 weeks of therapy. DESIGN AND METHODS: Retrospective virological analysis of an HIV-1/HBV co-infected lamivudine cohort derived from a randomized, placebo-controlled. . . lamivudine in HIV infection, the CAESAR study. RESULTS: Five of thirteen patients with HBV viral load > 10,000 copies/ml after **44**-52 weeks of lamivudine therapy had genotypic drug **resistance**. Four of these five had a rebound of viral replication over the period of study and in one case this was associated with an alanine transaminase serum elevation. Ten of the thirteen patients had

a 44-52 week HIV viral load > 1000 copies/ml, all of whom also had **HIV reverse transcriptase** M184V or M184I mutations. CONCLUSIONS: Extrapolating these results to the population yields an estimated 1-year incidence of drug-resistant HBV of. . . and virological benefit of HBV lamivudine monotherapy in co-infected patients should be balanced against the potential for emergence of drug **resistance**. Further, these data suggest that the determinants of HIV and HBV drug **resistance** are different and that parallel evolution, rather than co-evolution of HBV and HIV-1 in co-infected individuals occurs.

CT Check Tags: Human; Support, Non-U.S. Gov't
CD4 Lymphocyte Count
***Drug Resistance, Microbial**
HIV Infections: BL, blood
*HIV Infections: CO, complications
HIV Infections: IM, immunology
HIV-1: GE, genetics
HIV-1: IP, isolation. . .

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=> d his

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     FILE 'CAPLUS, MEDLINE' ENTERED AT 13:18:11 ON 02 DEC 2004
L1            81 FILE CAPLUS
L2           140 FILE MEDLINE
     TOTAL FOR ALL FILES
L3           221 S ((HIV (3W) (REVERSE TRANSCRIPTASE)) OR NTRI) AND RESISTANCE A
L4             1 FILE CAPLUS
L5             1 FILE MEDLINE
     TOTAL FOR ALL FILES
L6             2 S L3 AND (184 (3A) ((G OR GLY)  OR (L OR LEU)))

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L7             4 S (129:15939 OR 124:219374 OR 123:74260 OR 122:230221)/DN

     FILE 'CAPLUS, MEDLINE' ENTERED AT 14:09:40 ON 02 DEC 2004
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L10            1 S L3 AND (215 (3A) ((V OR VAL) ))
L11            0 FILE CAPLUS
L12            0 FILE MEDLINE
     TOTAL FOR ALL FILES
L13            0 S L3 AND (118 (3A) ((I OR ILE) ))
L14            3 FILE CAPLUS
L15            2 FILE MEDLINE
     TOTAL FOR ALL FILES
L16            5 S L3 AND (44 (3A) ((A OR ALA) OR (D OR GLU)))
L17            1 DUPLICATE REMOVE L6 (1 DUPLICATE REMOVED)

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